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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,299	10/25/2001	Stewart Thomas Leslie	208.1009	4506

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/037,299	LESLIE, STEWART THOMAS	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Papers Received: Remarks/Amendment dated 11/14/08

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 5-13, 16, 18 and 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee (WO 90/04965 hereafter referred to as '965). The claims are drawn to a transdermal composition comprising an opioid analgesic and distressing substance. The distressing substance is not permeable through the skin, yet will negate the opioid effects of the opioid if administered via bolus injection or oral delivery.

3. '965 discloses a transdermal preparation and device comprising opioid analgesics and opioid antagonists. The antagonist negates the analgesic properties of the opioid if the dosage form is delivered via bolus injection or oral delivery (abstract). The antagonist is not permeable through the skin in the transdermal presentation, and is incorporated with the same vehicle of the opioid analgesic (abstract). The transdermal device comprises an aqueous alcohol environment (example), a release liner and a backing layer (figures). The drugs listed as useful in the invention include fentanyl, buprenorphine butorphanol, cocaine and methadone (pg. 4, lin. 14 – 20). Antagonist include naloxone and naltrexone (pg. 4, lin. 21-25). Naloxone is well known as nauseants in opioid formulations and has severe side effects including severe headache, body

ache, withdrawal symptoms, vomiting and nausea. The device can be either a reservoir or a monolithic patch (figures). These disclosures render the claims anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 5-13, and 15-23 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lee (WO 90/04965 hereafter referred to as '965) in view of Blum et al (USPN 5,891,919 hereafter '919), Porter (USPN 4,175,119 hereafter '119). The claims are drawn to a transdermal formulation comprising an opioid analgesic such as buprenorphine and distressing agents such as an ergolide, bitter quaternary ammonium compounds or an emetic compound.

4. As discussed above the '965 patent discloses a transdermal patch formulation where an abusable opioid can be delivered and an opioid antagonist useful in deterring abuse is present in

the patch yet is not permeable through the skin. The antagonist causes nausea, vomiting and headaches when digested orally. The reference is silent to the specific deterring compound of the instant claims however. These compounds are well known in the art and it would have been obvious to include them into the '965 patent.

5. The '919 patent discloses a formulation comprising denatonium capsaicinate as a substance providing a bitter and/or spicy flavor for use as an aversive agent (Abstract). It may be incorporated into topical formulation and dressings and other pharmacological compositions (See Column 4, Lines 38-47). It would have been obvious to include the compound into the '538 formulation since this reference establishes the compounds use in aversion technologies.

6. The '119 patent discloses the use of an emetic to prevent accidental or intentional overdose of a psychoactive substance (Abstract, Column 1, lines 40-43). Such emetic substances include emetine hydrochloride, ipecamine, hydro-ipecamine and ipecacuanhin acid (Column 1, lines 52-57). It may be incorporated into formulation containing narcotic analgesics such as hydromorphone and codeine (Column 3, Lines 55-57). It would have been obvious to include the emetics into the '538 patent since both reference disclose the control of misusing the same compounds.

7. It would have been obvious to combine the bitter and emetic compounds of the '919 and '119 patents in order to provide a sufficient deterrent to potential misuse. The '965 patent discloses a transdermal formulation comprising opioid analgesics along with compounds that prevent abuse by ingestion or solvent extraction. These compounds included nauseants such as naloxone. The reference establishes the level of skill in the art regarding the inclusion of nauseants and distressing compounds into potential abusive compositions. The bitter/spicy

flavoring compounds of the '919 would cause distress if applied directly, and the emetics of the '119 would cause nausea upon exposure. It would have been obvious to combine the compounds in the transdermal formulation of the '965 with an expected result of a transdermal formulation useful in deterring misuse.

8. Claims 1, 2, 5-16, 18 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lee (WO 90/04965 hereafter '965) in view of Yum et al (USPN 6,001,390 hereafter '390) and Drugs: Facts and Comparisons, entry for *Pergolide Mesylate* pages 1621-1624.

9. As discussed above the '965 patent discloses a transdermal patch formulation where an abusable opioid can be delivered and an opioid antagonist useful in deterring abuse is present in the patch yet is not permeable through the skin. The antagonist causes nausea, vomiting and headaches when digested orally. The reference is silent to eh specific deterring compound of the instant claims however. These compounds are well known in the art and it would have been obvious to include them into the '965 patent.

10. The '390 patent a transdermal formulation comprising pergolide salts (abstract). The pergolides do not readily permeate through the skin and require permeation enhancers (col. 4, lin. 47-65). It would have been obvious to include the pergolide into the transdermal formulation of the '538 since they are similar formulations with similar components.

11. According to the *Pergolide* entry in the Drug textbook, the most common adverse reactions include nausea, dyskinesia, somnolence and rhinitis (page 1622). An artisan of ordinary skill would have been motivated to include the pergolide into the transdermal formulation of the '538 patent since the common side effects would negatively impact a user

upon misuse. Since the pergolides would not be permeable through the skin, they would act to deter misuse through injection or solvent distillation.

12. With these things in mind it would have been obvious include the ergot compounds of the '390 patent into the misuse deterring transdermal formulation of the '538 patent in order to provide sufficient deterrents to misuse. The side effects of pergolide salts are well known in the art as shown in the Drug textbook, and would have been an obvious addition to an aversion formulation. It would have been obvious to combine the teachings and formulations with an expected result of a transdermal formulation useful in treating pain without leading to potential abuse.

Response to Arguments

Applicant's arguments with respect to claims 1, 2, and 5-23 have been considered but are moot in view of the new ground(s) of rejection. However the '919, '119 and '390 patents remain as supporting references since they teach the specific abuse deterring compounds of the instant claims. The '965 patent was previously applied and as a result of the claim amendments, reads on the instant claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 7:00-4:30; every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618
/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618